

CLAIMS

What is claimed is:

1. A method of modulating ciliary neurotrophic factor cell signaling activity in a cell, comprising contacting said cells with an modulator of SOCS-3 activity.
- 5 2. The method of Claim 1 wherein SOCS-3 activity is inhibited, resulting in increased ciliary neurotrophic factor cell signaling activity.
3. The method of Claim 2 wherein the expression of SOCS-3 protein is inhibited, comprising introducing a nucleotide construct comprising a polynucleotide wherein the polynucleotide prevents transcription of SOCS-3 DNA.
- 10 4. The method of Claim 2 wherein the expression of SOCS-3 protein is inhibited, introducing a nucleotide construct comprising a polynucleotide encoding SOCS-3 antisense nucleotide into a cell, wherein the antisense SOCS-3 nucleotide acid binds to endogenous SOCS-3 mRNA in the cell, thereby inhibiting expression of SOCS-3 protein.
- 15 5. The method of Claim 2, comprising introducing a nucleotide construct encoding a modified SOCS-3 polypeptide into the cell, wherein the modified SOCS-3 polypeptide is a competitive inhibitor of endogenous SOCS-3, thereby inhibiting SOCS-3 activity.
6. The method of Claim 2, comprising introducing a SOCS-3 inhibitor into a cell, 20 wherein the inhibitor interferes with the interaction of SOCS-3 with a SOCS-3 target protein.

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7. The method of Claim 6, wherein the SOCS-3 target protein is JAK2.

8. The method of Claim 1, wherein SOCS-3 activity is increased, resulting in decreased ciliary neurotrophic factor cell signaling activity.

9. The method of Claim 8, wherein the expression of SOCS-3 protein is increased.

10. The method of Claim 9, comprising introducing into a cell a nucleotide construct encoding a SOCS-3 polypeptide or a modified SOCS-3 polypeptide.

11. A cell line comprising a cytokine receptor and a reporter gene construct, wherein contacting said cytokine receptor with its cognate ligand results in SOCS-3 production, and wherein transcription of the reporter gene is inhibited by SOCS-3.

12. The cell line of Claim 11, wherein the reporter gene construct contains SOCS-3 promoter elements.

13. The cell line of Claim 11, wherein the cytokine receptor is the ciliary neurotrophic factor receptor.

14. A method for identifying inhibitors of SOCS-3 activity, comprising the steps of:

a) contacting the cells of Claim 11 with an organic molecule library comprising candidate SOCS-3 inhibitors or transfecting said cells with a cDNA expression library comprising DNA encoding candidate SOCS-3 inhibitors;

b) contacting the cells of step a) with ciliary neurotrophic factor;

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- c) selecting the cells of step b) having increased reporter gene activity; and
- d) identifying the organic molecule or cDNA selected in step c).

15. A SOCS-3 inhibitor identified by the method of Claim 14.

16. A ciliary neurotrophic factor responsive cell line, wherein the cell line is
5 dependent upon a second cytokine for growth.

17. The cell line of Claim 16, wherein the second cytokine is IL-3.

18. A method for identifying inhibitors of SOCS-3 activity comprising the steps of:
a) culturing the cells of Claim 17 in the presence of IL-3 under conditions
10 suitable for growth;
b) removing the cells of step a) from the presence of IL-3;
c) contacting the cells of step b) with an organic molecule library comprising
candidate SOCS-3 inhibitors or transfecting said cells with a cDNA
expression library comprising candidate SOCS-3 inhibitors;
d) contacting the cells of step c) with ciliary neurotrophic factor;
15 e) selecting the cells of d), that are capable of proliferating in the presence of
ciliary neurotrophic factor; and
f) identifying the organic molecule or cDNA selected in e).

19. A SOCS-3 inhibitor identified by the method of Claim 18.

20. A method of reducing weight or food intake in a mammal, comprising
20 administering an effective amount of a SOCS-3 inhibitor to said mammal.

21. A method of reducing weight or food intake in a mammal, comprising administering an effective amount of ciliary-neurotrophic factor in combination with a SOCS-3 inhibitor to said mammal.

22. A method of preventing or inhibiting neurodegeneration in a mammal, comprising administering an effective amount of a SOCS-3 inhibitor to said mammal.

5 23. A method of preventing or inhibiting neurodegeneration in a mammal, comprising administering an effective amount of ciliary neurotrophic factor in combination with a SOCS-3 inhibitor to said mammal.

10 24. A method of increasing weight or food intake in a mammal, comprising administering an effective amount of ciliary neurotrophic factor inhibitor to said mammal.

25. The method of Claim 24, wherein SOCS-3 activity is enhanced.

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